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AWARD NUMBER: DAMD17-01-1-0124

TITLE: Selenium and Breast Cancer Chemoprevention

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REPORT DATE: December 2005

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE

*Form Approved
OMB No. 0704-0188*

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1. REPORT DATE (DD-MM-YYYY) December 2005			2. REPORT TYPE Annual		3. DATES COVERED (From - To) 1 Aug 04 – 30 Nov 05	
4. TITLE AND SUBTITLE Selenium and Breast Cancer Chemoprevention			5a. CONTRACT NUMBER			
			5b. GRANT NUMBER DAMD17-01-1-0124			
			5c. PROGRAM ELEMENT NUMBER			
6. AUTHOR(S) Henry J. Thompson, Ph.D. E-Mail: henry.thompson@colostate.edu			5d. PROJECT NUMBER			
			5e. TASK NUMBER			
			5f. WORK UNIT NUMBER			
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Colorado State University Fort Collins, Colorado 80523-2002			8. PERFORMING ORGANIZATION REPORT NUMBER			
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSOR/MONITOR'S ACRONYM(S)			
			11. SPONSOR/MONITOR'S REPORT NUMBER(S)			
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited						
13. SUPPLEMENTARY NOTES						
14. ABSTRACT The primary objective of this project is to determine whether selenium supplementation affects candidate markers of breast cancer risk in a cohort of women at elevated risk for breast cancer. The intermediate biomarkers being studied are: indicators of oxidative damage to cellular macromolecules such as DNA and lipid, indicators of IGF metabolic status, and cellular indicators of breast cancer risk. We proposed a randomized, placebo-controlled, double-blind chemoprevention trial with 150 participants (75 subjects per arm) using a placebo tablet or a tablet containing 200 µg high-selenium brewer's yeast per day, given for a duration of one year. The form and dose of selenium that is being used has been reported to reduce cancer incidence and mortality in lung, prostate, and colon. Blood and urine is being collected at baseline, and after 6 and 12 months of intervention. The feasibility of obtaining breast epithelial cells via nipple aspiration at baseline and the end of the intervention is being assessed. Plasma selenium and glutathione peroxidase activity are being evaluated in addition to pill counts and self report as markers of compliance.						
15. SUBJECT TERMS Breast Cancer, Prevention, Chemoprevention, Selenium, Oxidative Damage, IGF-1						
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC	
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U	UU	6	19b. TELEPHONE NUMBER (include area code)	

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Introduction

The primary objective of this project is to determine whether selenium supplementation affects candidate markers for breast cancer risk in a cohort of women at elevated risk for breast cancer. The intermediate biomarkers being studied are: indicators of oxidative damage to cellular macromolecules such as DNA and lipid, indicators of IGF metabolic status, and cellular indicators of breast cancer risk.

Body of Report

Approved Statement of Work

We are conducting a randomized, placebo-controlled, double-blind chemoprevention trial with 150 participants (75 subjects per arm) using a placebo tablet or a tablet containing 200 µg high-selenium brewer's yeast per day, given for a duration of one year. Blood and urine are being collected at baseline, and after 6 and 12 months of intervention. Efforts are being made to obtain breast epithelial and/or breast fluid via nipple aspiration using a modified breast pump. This procedure is performed at baseline and the end of the intervention. Randomization will be in 15 blocks of 10 subjects each.

1. Year 01

- a. Final development of project materials including Web-based randomization program, data entry screens, data quality assurance procedures, project databases.
- b. Obtain all supplements.
- c. Initiate recruitment and enter 3 blocks of 10 subjects.
- d. Schedule follow-up visits.
- e. Institute monthly patient follow-up.
- f. Ongoing collection and analyses of biological samples.
- g. Enter results into databases.
- h. Submit progress report.

2. Years 02-03

- a. Enter remaining subjects into the study and continue follow up, sample collection and analyses.
Goal is 8 blocks of 10 in year 02 and 4 blocks of 10 in year 03.
- b. Submit progress reports.

3. Year 04

- a. Complete follow up and the collection and analysis of all samples.
- b. Evaluate all data.
- c. Summarize findings for publication and submit final report.

No Cost Extension A one year no cost extension was requested and approved. The project will end December 31, 2006.

Acronym for Study We refer to this project as the ENRICH study.

Progress on Year 04 Objectives

a. Accrual Completed

As of July 1, 2005, 162 women had been enrolled in the project and project accrual was closed. Accrual was allowed to exceed target enrollment (150) to compensate for a slightly higher than expected dropout rate. The average Gail Score of the women enrolled was 3.0 (5-year risk) and mean breast density was 54%. Both values are consistent with this cohort being at increased risk for breast cancer .

b. Ongoing clinical work

As of November 30, 2005 45 women had not yet completed the clinical protocol. The last participant will complete the study in June, 2006.

c. Compliance Pill count data indicate that compliance is in excess of 97%. Plasma selenium analysis by group is consistent with high compliance; there is very little overlap in the two distributions. Moreover, the maximum plasma selenium levels being measured also indicate that participants are well within safe and acceptable levels of intake.

d. Nipple Aspirate Fluid In the year 01 Annual Report, we noted the difficulty of obtaining nipple aspirate fluid from many participants and when it was obtained the problem of the adequacy of the cellular content for cytological analyses. Our current rate of success in obtaining NAF is 30%. Cell content remains low and for this reason, we continue to work on the use of proteomic analysis of either NAF or serum as a biomarker for cancer risk that would replace cytological analysis of NAF in evaluating the effect(s) of selenium on disease risk.

e. Routine biostatistical audit The most recent audit conducted by the project biostatistician indicates that the accuracy of data entry into the database is above 95%. There were no errors detected in the random sample audited.

c. Submit progress report. This document

Key Research Accomplishments Enrollment has been completed. The clinical component of the study will be completed in June 2006. Because of the double-blind study design, no biological data is currently available.

Reportable Outcomes (cumulative)

- Supporting intervention materials were developed and tested (when appropriate).
- The project database was completed
- The intervention phase of the project is being completed.

Conclusions Work is progressing as planned with continuing attention focused on completing the clinical phase of the study and analyzing biological specimens that have been collected. The data obtained will be evaluated and interpreted once the clinical phase of the study has been completed.

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